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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/563,480	01/05/2006	Giuseppe Giannini	ARC-4865-103	1355

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NIXON & VANDERHYE, PC
901 NORTH GLEBE ROAD, 11TH FLOOR
ARLINGTON, VA 22203

EXAMINER	
SHIAO, REI TSANG	

ART UNIT	PAPER NUMBER
1626	

MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/563,480	GIANNINI ET AL.	
	Examiner	Art Unit	
	REI-TSANG SHIAO	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 May 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10 and 13-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10 and 13-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *05 January 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1/5/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. This application claims benefit of the foreign application:

UNITED KINGDOM 0316910.9 with a filing date 07/18/2003.

2. Amendment of claims 1, 10, and 13-18, cancellation of claims 11-12, and addition of claim 20 in the amendment filed on May 20, 2008 is acknowledged. Claims 1-10 and 13-20 are pending in the application. No new matter has been found. Since the newly added claim 20 is commensurate with the scope of the invention, claims 1-10 and 13-20 are prosecuted in the case.

Information Disclosure Statement

3. Applicant's Information Disclosure Statement, filed on January 05, 2006 has been considered. Please refer to Applicant's copy of the 1449 submitted herein.

Responses to Election/Restriction

4. Applicant's election of Group II claims 1-19, in part, (now are 1-10 and 13-20) in the reply filed on May 20, 2008 is acknowledged. Election of a compound, i.e., (Z)-1,2-difluoro- 1-(3,4,5-trimethoxyphenyl)-2-(3-hydroxy-4-methoxyphenyl)ethane o-disodium phosphate (ST2493) as the single species is also acknowledged.

Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 1-10 and 13-20 are pending in the application. The scope of the invention of the elected subject matter is as follows.

Claims 1-10 and 13-20, drawn to compounds/compositions of formula (I), and their methods of use.

The requirement is still deemed proper.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 13-18 and 20 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for using compounds of formula (I) for treating lung carcinoma, it does not reasonably provide enablement for treating non-neoplastic disease or treating tumor without limitation (i.e., no named tumor), see claim 13 or 20. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

In *In re Wands*, 8 USPQ2d 1400 (1988), factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described. They are:

1. the nature of the invention,

2. the state of the prior art,

3. the predictability or lack thereof in the art,

4. the amount of direction or guidance present,

5. the presence or absence of working examples,

6. the breadth of the claims,

7. the quantity of experimentation needed, and

8. the level of the skill in the art.

In the instant case:

The nature of the invention

The nature of the invention of claims 13-18 and 20 are drawn to intent methods of use using compounds of formula **(I)** for treating non-neoplastic disease or treating tumor without limitation (i.e., no named tumor), see claim 13 or 20.

The state of the prior art and the predictability or lack thereof in the art

The state of the prior art is that the pharmacological art involves screening *in vitro* and *in vivo* to determine which compounds exhibit the desired pharmacological activities (i.e. what compounds can treat which specific diseases by what mechanism). There is no absolute predictability even in view of the seemingly high level of skill in the art. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic or preventive regimen on its face.

The instant claimed invention is highly unpredictable as discussed below:

It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. *In re Fisher*, 427 F.2d 833,166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute.

Applicants are claiming intent methods of use using compounds of formula (I) effective to treat non-neoplastic disease or treat a tumor without limitation (i.e., no named tumor). As such, the specification fails to enable the skilled artisan to use the compounds of claims effective to treat various tumors.

In addition, there is no established correlation between *in vitro* or in *vivo* activity and accomplishing treatment of various diseases, and those skilled in the art would not accept allegations in the instant specification to be reliable predictors of success, and those skilled in the art would not be able to use compounds of formula (I) since there is no description of an actual method wherein various tumors in a host is treated.

Hence, one of skill in the art is unable to fully predict possible results from the administration of the compounds of formula (I) due to the unpredictability of the various diseases. The "treating tumors" without limitation is known to have many obstacles that would prevent one of ordinary skill in the art from accepting treating regimen on its face.

The amount of direction or guidance present and the presence or absence of working examples

The only direction or guidance present in the instant specification is the listing of

in vitro assay in cells, in terms of IC_{50}, and animal model of lung cancer, see pages 23-26 of the specification. There are no *in vitro* or *in vivo* working examples present for the treatment of non-plastic disease or tumors without limitation by the administration of the instant invention.

The breadth of the claims

The breadth of the claims is methods of use of the instant compounds effective to treat non-plastic disease or treat various tumors other than lung carcinoma.

The quantity of experimentation needed

The quantity of experimentation needed is undue experimentation. One of skill in the art would need to determine what diseases would be benefited (i.e., treated) by the administration of the instant invention and would furthermore then have to determine which of the claimed methods of use would provide treatment of a tumor, if any.

The level of the skill in the art

The level of skill in the art is high. However, due to the unpredictability in the pharmaceutical art, it is noted that each embodiment of the invention is required to be individually assessed for physiological activity by *in vitro* and *in vivo* screening to determine which methods of use exhibit the desired pharmacological activity and which diseases would benefit from this activity. Thus, the specification fails to provide sufficient support of the broad use of the pharmaceutical compounds of the instant claims for the various diseases.

As a result necessitating one of skill to perform an exhaustive search for which diseases, can be treated by what pharmaceutical compounds of the instant claims in order to practice the claimed invention. Thus, factors such as "sufficient working examples", "the level of skill in the art" and "predictability", etc. have been demonstrated to be sufficiently lacking in the instantly claimed methods. In view of the breadth of the claim, the chemical nature of the invention, and the lack of working examples regarding the activity of the claimed compounds in regards to the treatment of the many diseases resulting from "inhibiting tubulin polymerization", one having ordinary skill in the art would have to undergo an undue amount of experimentation to use the invention commensurate in scope with the claims.

Genentech Inc. v. Novo Nordisk A/S (CA FC) 42 USPQ2d 1001, states that " a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable".

Therefore, in view of the Wands factors and *In re Fisher* (CCPA 1970) discussed above, to practice the claimed invention herein, a person of skill in the art would have to engage in undue experimentation, with no assurance of success. This rejection can be overcome by incorporation of the limitation of tumor (i.e., lung carcinoma) and deletion of claim 20 would obviate the rejection.

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-10 and 13-20 are rejected under 35 U.S.C. 102(b) as being anticipated by Tsai's CAS: 124:231924.

Applicants claim compounds of formula (I), see claim 1.

Tsai's disclose two compounds, see RN: 174810-57-2 or 174810-58-3. They clearly anticipate the instant compounds of formula (I), wherein the variable Y is halogen (I.e., F), the variable R is OH, the variables Z, or R1-R3 independently represent H. Dependent claims 2-10 and 13-20 are also rejected along with claim 1 under 35 U.S.C. 102(b).

Claims Objection

7. Claim 4 is objected to because of the following informalities: a term "and" or a symbol ";" is missing at the end of the last second compound. Moreover, a symbol "." is missing at the end of the claim. Incorporation of a term "and" and a symbol ";" after the second named compound would obviate the objection.

8. Claim 1, line 11, recites the term "their pharmaceutical acceptable salts, recemates and single enantiomers" is objected. Replacement of the term "their pharmaceutical

acceptable salts, recemates and single enantiomers" with a term "its pharmaceutical acceptable salt, recemate and single enantiomer"" would obviate the objection.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rei-tsang Shiao whose telephone number is (571) 272-0707. The examiner can normally be reached on 8:30 AM - 5:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph K. McKane can be reached on (571) 272-0699. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/REI-TSANG SHIAO /

Rei-tsang Shiao, Ph.D.
Primary Patent Examiner
Art Unit 1626

September 24, 2008